Provider Information: Gardasil® 9 VIS

Many Vaccine Information Statements are available in Spanish and other languages. See www.immunize.org/vis.

Gardasil 9 is a 9-valent vaccine for prevention of disease caused by 9 types of human papillomavirus: HPV types 6, 11, 16, 18, 31, 33, 45, 52, & 58.

Gardasil (quadrivalent) contains types 6, 11, 16, & 18. At this time, both Gardasil and Gardasil 9 are available, and either may be used.

Gardasil 9 is recommended for **females** for the prevention of cervical, vulvar, vaginal and anal cancers and genital warts caused by these human papillomavirus types, and for **males** for the prevention of anal cancer and genital warts caused by these human papillomavirus types.

Burden of Disease Associated with HPV Vaccine Types

	HPV Type	Cervical Cancer	All HPV-Associated Cancers	Anogenital Warts	
Gardasil	6			90%	Gardasil 9
	11				
	16	66%	64%		
	18				
	31	15%	10%		
	33				
	45				
	52				
	58				

Gardasil 9 is approved by FDA for males and females 9 through 26 years of age. Note: Gardasil 9 was originally approved for males through age 15 only, and CDC's recommendations for vaccinating older males were off-label. But on December 14, 2015, FDA approved the vaccine for males through age 26.

Age Recommendations:

- **Age 11 or 12:** Recommended ages for routine vaccination.
- **Age 9 and 10:** May be given at the discretion of the provider.
- **Age 13 through 26 (females):** Recommended, if not given at the routine age.
- **Age 13 through 26 (males):**
  - Recommended for all males through age 21, if not given at routine age.
  - Recommended for MSM, males with immune deficiencies, and HIV-infected males (regardless of their immune status) through age 26.
  - *May* be given to all males through age 26.

Schedule:

The recommended schedule is **3 doses**

- **First Dose**: Any time during recommended age range.
  - Routinely recommended at 11-12 years of age.
- **Second Dose**: 1-2 months after the first.*
  - *Minimum interval* after first dose = 4 weeks.
- **Third Dose**: 6 months after the first.
  - *Minimum interval* after second dose = 12 weeks
  - *Minimum interval* after first dose = 6 months

  NOTE: The FDA-approved interval between the first and second doses of Gardasil 9 is **2 months. However, ACIP has harmonized the schedules for Gardasil, Gardasil 9 and Cervarix (for which the approved interval is 1 month), recommending that the 2nd dose may be given at either **1 or 2 months** after the 1st for any HPV vaccine.*
- Gardasil 9 may be given concurrently with other vaccines indicated during the same time frame.

Special Circumstances:

- People who started or completed a series with quadrivalent or bivalent HPV vaccine (Gardasil or Cervarix)
  - A person who has received one or two doses of another HPV vaccine may complete the series with Gardasil 9.
  - There is no recommendation at this time for administering Gardasil 9 to a person who has completed a 3-dose series with another HPV vaccine.
- Pregnant Women
  - Gardasil 9 is not recommended for use in pregnant women.
  - Pregnancy testing is not necessary before vaccination, but if a woman is found to be pregnant after the vaccine series has been initiated, the remaining doses should be delayed until after delivery. It is not necessary to restart the series.
  - If the vaccine is administered during pregnancy, no intervention is needed.
  - Women who receive Gardasil 9 around the time of conception or during pregnancy are encouraged to contact the manufacturer's Pregnancy Registry at 1-800-986-8999, to allow monitoring of outcomes of pregnant women exposed to the vaccine.
  - Published data have not found any safety concerns among pregnant women who have been inadvertently vaccinated.

Contraindications and Precautions

Contraindications:

- "The only contraindication applicable to all vaccines is a history of a severe allergic reaction (i.e., anaphylaxis) after a previous dose of [the] vaccine or to a vaccine component" (ACIP *General Recommendations on Immunization*). *Anaphylaxis following a dose of quadrivalent Gardasil is also a contraindication to Gardasil 9.*

  Components of the Gardasil 9, from the December 2014 package insert, are:
  - yeast protein
  - vitamins
  - amino acids
  - mineral salts
  - carbohydrates
  - amorphous aluminum hydroxyphosphate sulfate
  - L-histidine
  - polysorbate 80
  - sodium borate

  Gardasil 9 vials and syringes do not contain latex.

Precautions:

- "The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines." (ACIP *General Recommendations on Immunization*) The definition of "moderate or severe acute illness" is left to the clinical judgment of the provider. A vaccination deferred because of an acute illness should be rescheduled after the illness has resolved.

Safety

The vaccine was well-tolerated in clinical trials. The most common local and systemic adverse events after any dose of Gardasil 9 were injection-site related pain, swelling, erythema, headache, and pyrexia that were mild to moderate in intensity:

Adverse Event	Females 9-15 Years of Age	Females 16-26 Years of Age	Males 9-15 Years of Age
Pain	89%	90%	72%
Swelling	48%	40%	27%
Erythema	34%	34%	25%
Headache	11%	15%	9%
Temperature ≥100°F	7%	6%	10%
Temperature ≥102°F	1%	1%	-

Rates of adverse events can vary depending on which dose of the series is given. For a more detailed analysis of adverse events, see the manufacturer's package insert.

85 million doses of HPV vaccine were distributed in the US from June 2006 through September 2015. No new safety concerns were identified during post-licensure vaccine safety monitoring.

HPV vaccine safety findings are similar to those identified in safety reviews of meningococcal and Tdap vaccines.

Most commonly reported non-serious possible side effects are:

- Pain, redness, or swelling in the arm where the shot was given
- Fever
- Headache or feeling tired
- Nausea
- Fatigue
- Dizziness

A study was conducted through CDC's Vaccine Safety Datalink, looking at 9 conditions (Guillain-Barré syndrome, seizures, syncope, appendicitis, stroke, venous thromboembolism, anaphylaxis, and other allergic reactions). After 600,558 doses of (quadrivalent) Gardasil had been administered to females, no statistically significant associations were found among those who received HPV vaccination compared with those who were unvaccinated or who received other vaccines. Other large epidemiologic studies have been reassuring on the safety of HPV vaccines.

Some deaths among persons who received HPV vaccine have been reported to the Vaccine Adverse Event Reporting System (VAERS). All reports of death are reviewed by medical doctors at CDC or FDA. While not all death reports can be verified because not enough information was reported, detailed review of every report of death following of Gardasil vaccine has shown:

1. There is no pattern of death occurring with respect to time after vaccination.
2. There is no consistent vaccine dose number or combination of vaccines given.
3. There is no diagnosis at death that would suggest that the Gardasil vaccine caused the death.

Problems that could happen after any vaccine:

A 2012 Institute of Medicine report titled *Adverse Effects of Vaccines: Evidence and Causality* concluded that evidence supports a causal relation between injection of vaccines and both **syncope** and **deltoid bursitis**. In both cases, IOM determined that the injection itself, and not the contents of the vaccine, contributes to the development of these adverse events.

For more information, see the following ACIP recommendation:

"Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices" (March 27, 2015)
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6411a3.htm

"Human Papillomavirus Vaccination: Recommendations of the Advisory Committee on Immunization Practices (ACIP)" (August 29, 2014)
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6305a1.htm

December, 2015